

NICEATM

*National Toxicology Program
Interagency Center for the Evaluation of
Alternative Toxicological Methods*

ICCVAM

*Interagency Coordinating Committee on
the Validation of Alternative Methods*

Summary of the Independent Scientific Peer Review Panel Evaluation of the Validation Status of the LUMI-CELL[®] ER (BG1LUC ER TA) Test Method



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Review Panel

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ICCVAM Charges to the Peer Panel

- Review the ICCVAM draft BRD for completeness and identify any errors or omissions
- Determine the extent to which the ICCVAM criteria for validation and acceptance have been appropriately addressed
- Consider the ICCVAM draft test method recommendations for the following and comment on the extent to which they are supported by the information provided in the BRD:
 - Proposed test method usefulness and limitations
 - Proposed recommended standardized protocols
 - Proposed test method performance standards
 - Proposed future studies



Peer Panel Report – May 16, 2011

- These are abbreviated highlights of the final Independent Scientific Peer Review Panel report
 - The final report should be consulted for a detailed description of the Panel's conclusions and recommendations
 - <http://iccvam.niehs.nih.gov/methods/endocrine/PeerPanel11.htm>

The LUMI-CELL® ER Method

- Generically referred to as the BG1Luc ER TA test method
- *In vitro* test method - human ovarian cancer cells
 - Proposed as an initial screen to identify substances with the potential to enhance or inhibit activity of the estrogen receptor



Peer Review Panel Recommendations: Usefulness and Limitations

- The Panel agreed with ICCVAM that the BG1Luc ER TA test method can be used as a screening test to identify substances with in vitro estrogen agonist and antagonist activity
 - Because there has been no clear regulatory guidance on how ER TA test methods will be used in the EPA EDSP, the use of the BG1Luc ER TA in the overall strategy of hazard or safety assessment of endocrine active chemicals is unclear
- The BG1Luc ER TA method could be considered as a replacement for the EPA ER TA method and the rat uterine cytosol (RUC) binding assays
 - However, the Panel noted that additional analysis could be necessary to further support this recommendation, particularly regarding the RUC ER binding assay



Peer Review Panel Recommendations: Test Method Protocol

- The Panel considered the BG1Luc ER TA test method protocol complete and adequate in detail
- Also noted several advantages over the ER TA method currently used in the EPAs EDSP for this endpoint:
 - Robust test method protocol
 - Valid for testing up to 1 mM (per EPA's requirements)
 - Can detect substances with both in vitro estrogenic and anti-estrogenic activity

Peer Review Panel Recommendations: Future Studies

- The Panel agreed with the draft ICCVAM recommended future studies
- The Panel also suggested additional activities:
 - Studies to account for metabolic activation
 - Expanding the reference substance list and associated BG1Luc ER TA database with additional negative agonist and positive antagonist test substances as they are identified
 - Recognizing they currently are not available and/or have yet to be identified
 - Efforts to identify a quantitative cytotoxicity method



Peer Review Panel Recommendations: Performance Standards

- The Panel concurred with the draft ICCVAM Performance Standards
- The Panel also proposed modifications that could expand the Performance Standards applicability including:
 - For example, specific tissue source and type may not be critical
 - More negative agonist and positive antagonist reference substances should be included – when available
 - Reference classification should be based upon literature reports that have been ranked with a method that focuses on the reliability of the published data



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Questions?



SACATM Discussion Questions

1. Do you have any comments on the Peer Review Panel report and its conclusions and recommendations regarding the validation status of the LUMI-CELL[®] ER (BG1Luc ER TA) Test Method?
2. Do you have any comments on the draft Background Review Document or draft Performance Standards?

